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Screening Peter to Save Paul: The population-level effects of screening MSM for gonorrhea and chlamydia

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Screening has been a cornerstone of sexually transmitted disease (STD) prevention programs for decades, and continues to be a priority public health activity at the local, state, and federal levels in the United States^{1,2} and for other international public health agencies^{3–8}. However, developing the evidence base for promotion and scale-up of bacterial STD screening among men who have sex with men (MSM) has been challenging, as highlighted in the paper by Tsoumanis and colleagues⁹ in this issue of *Sexually Transmitted Diseases*. In their paper, Tsoumanis et al. attempt to evaluate if screening for chlamydia and gonorrhea in MSM is associated with a reduction of the prevalence of these infections using a systematic literature review approach. Although Tsoumanis et al. abstracted data from a range of published sources, it difficult to draw robust inferences and conclusions from their review, owing to limitations associated with their analytic approach, their interpretation of published findings, and the studies they reviewed. Nevertheless, we agree with Tsoumanis et al. in their assessment that there is little empirical evidence of the effectiveness of STD screening to reduce population-level STD prevalence among MSM. Further, their literature review provides an opportunity to reflect on why we screen individuals for STDs, how we measure the impact of STD screening, and how we can better evaluate the population-level benefits of STD screening in the absence of good data.

Why do we screen individuals for STDs?

There are some proven individual level benefits to STD screening for women and their babies, and likely some for MSM. For example, routine screening of young women for

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chlamydia is a cost-effective way to prevent pelvic inflammatory disease^{10–12} and screening pregnant women for syphilis prevents most vertical transmission¹³. Screening also provides an opportunity to provide additional prevention services, such as substance abuse and mental health referrals¹⁴. For MSM, although not well documented, individual-level benefits of screening for gonorrhea and chlamydia could include reduction in complications (e.g., disseminated gonococcal infection) and a reduction in HIV acquisition^{15, 16}. Additionally, screening HIV-uninfected MSM could act as an entry point to HIV-prevention services like preexposure prophylaxis (PrEP), [15] and screening HIV-infected MSM could provide an opportunity to engage MSM living with HIV into care¹⁷.

Additionally, there may be population-level benefits to screening, although this has been even less well documented. Screening and appropriate treatment can eliminate an individual's infection in anatomic reservoirs such as the rectum and pharynx. As many of these infections are asymptomatic, detecting and treating infections in these reservoirs might help reduce ongoing transmission, possibly reducing prevalence in the population¹⁸. Furthermore, the pharynx may be important in the development and transmission of antibiotic-resistant gonorrhea^{19, 20}. Because many pharyngeal gonococcal infections are asymptomatic, screening might also help prevent the development and ongoing transmission of antibiotic-resistant gonorrhea.

How do we measure the impact of STD screening?

Well-designed and properly powered randomized control trials are the gold standard for measuring the impact of an intervention²¹. When developing screening recommendations, the U.S. Preventive Services Task Force (USPSTF) reviews published evidence of the effectiveness of screening compared with not screening on individual-level outcomes, specifically benefits (reduction of complications of infection and transmission or acquisition of disease) and potential harms (labeling, anxiety, false-positive and false-negative test results)²². As Tsoumanis et al. discuss, USPSTF conducted a systematic review for chlamydia and gonorrhea and concluded “that current evidence is insufficient to assess the balance of benefits and harms of screening for gonorrhea/chlamydia in MSM”^{9, 22}. It is important to note that the USPSTF review found no studies that met the inclusion criteria to evaluate the individual-level benefits and harms of screening for gonorrhea, and only 3 for chlamydia screening (all among women). This lack of evidence does not mean that screening men, including MSM, does not have individual-level benefits, but that there have been no adequate studies to evaluate the individual-level benefits of screening among men.

The lack of published evidence for the individual-level benefit of screening MSM for chlamydia and gonorrhea is not surprising. Although there may be individual-level benefits, there are a number of challenges to conducting randomized controlled trials to quantify the benefit of screening in this population. Adverse outcomes associated with gonorrhea and chlamydia in men are rare; thus, a prospective study would require a large sample size to be adequately powered to identify negative sequelae. Additionally, given highly effective biomedical interventions for the prevention of HIV infection (e.g., PrEP, antiretroviral treatment as prevention), it is increasingly difficult to demonstrate protective effects of STD screening interventions when HIV infection is the outcome of interest²³. Furthermore,

extragenital infections are an important reservoir for chlamydia and gonorrhea among MSM, yet few published studies have evaluated the impact of extragenital screening.

It is important to keep in mind that USPSTF reviews focus exclusively on individual-level impact of an intervention, and explicitly do not focus on population-level impact. Although not considered in the USPSTF review of evidence, there may be additional population-level effects of screening, including a reduction in population prevalence. Evaluating population impact would require a community randomized trial or data from a population-based sample before and after a change in STD screening policy. Unfortunately, these data are scarce and there is a low likelihood that a community-level randomized control trial will ever be conducted to evaluate the effects of screening, as the scale and cost would be prohibitive.

Tsoumanis et al. attempted to evaluate if screening MSM for gonorrhea and chlamydia decreases the prevalence of these infections in the population using available data. Unfortunately, the majority of studies included in the Tsoumanis review did not measure the population prevalence of disease, nor did they evaluate a change in STD screening practices. Additionally, the data they were able to identify consisted mainly of small cohort studies or convenience samples with a small number of individuals, which were not representative of the population. In fact, none of the studies included in their literature review was designed to evaluate the population-level effects of STD screening among MSM. For example, Grant et al.²⁴ was designed to compare HIV incidence in a PrEP versus placebo group and was not designed to look at STD changes over time and the study's authors provide no interpretation or conclusion about the numbers of STD reported. Furthermore, the Tsoumanis et al. review was subject to errors in interpretation of data from published studies, such as interpreting reported cumulative incidence as prevalence. Consequently, it is difficult to interpret findings from Tsoumanis's review.

How can we evaluate the population benefits of STD screening in the absence of good data?

The question that Tsoumanis et al. aimed to answer, namely whether screening MSM for gonorrhea and chlamydia decreases the prevalence of these infections in the population, is important but difficult to answer. Tsoumanis et al.'s review sparks some critical questions for the field. Is there sufficient equipoise to randomize some individuals to not receive STD screening? Should the focus of evaluation of STD screening for MSM be at the individual-level or population-level benefits of screening, or both? Given the lack of currently available evidence, we may have to think more creatively about potential ways to evaluate this question. We found one study not included in the Tsoumanis' review (Barry, et al.²⁵) that looked at the population-level impact of STD screening in jails on chlamydia rates among females in community clinics. Barry et al found that jail screening of young adults focused in neighborhoods with high chlamydia rates was followed by a decline of chlamydia among young females at a clinic serving neighborhoods with high jail testing density. Though no direct causal inferences can be made, as no direct link was documented between persons screened in jail and females screened in the neighborhood clinics, jails could be an efficient method for identifying and treating STDs unlikely to be diagnosed elsewhere. The potential

for STD screening in jails to reduce STD prevalence in the population has been demonstrated by mathematical models of STD transmission²⁶. Indeed, modeling has been and continues to be an important tool for estimating the potential population-level effects of a range of STD screening interventions. However, it is time to think of novel approaches to evaluate the population benefits of STD screening. In the meantime, there remains no existing evidence that we should change our current STD screening recommendations.

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